REMARKS

Prior to the present amendment, claims 11, 12, and 36 were pending. By the present amendment, claim 36 was amended and claim 12 was cancelled. Accordingly, claims 11 and 36 are currently pending.

AMENDMENTS

Claim 36, as amended, specifies that the composition comprises a single active component that reduces cutaneous facial flushing. The single active component consists of brimonidine tartrate.

The purpose of the amendment is to ensure that the claimed composition only contains one single active component that reduces cutaneous facial flushing. The claim language is meant to exclude any other active components that reduce cutaneous facial flushing from the composition.

The claim was also amended to overcome the examiner's 35 U.S.C. 112, first paragraph, rejection, which is discussed below.

Support for the single active component consisting of brimonidine tartrate can be found throughout the specification as filed, for example on page 1, lines 11, 12; page 4, lines 14, 15, 19, 20, 25; page 5, line 3; page 6, lines 4, 17, and 29; the sentence bridging pages 5 and 6; and page 7, line 5-7; as well as claims 2, 13, 22, 25, 27, and 28 as originally filed.

No new matter has been added by the amendments to the claims.

37 CFR 1.75 OBEJCTION

The examiner objected to claim 12 under 37 CFR 1.75 as being a substantial duplicate of claim 11. Accordingly, applicant has cancelled claim 12.

35 U.S.C. 112, FIRST PARAGRAPH, REJECTION

The examiner rejected claims 11, 12, and 36 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. According to the examiner, the specification and claims as originally filed fail to provide adequate written description for the limitation directed to the use of brimonidine *per se* or combinations of brimonidine and brimonidine tartrate (claim 36).

The examiner, however, acknowledges that the specification as filed supports claims directed to brimonidine tartrate (i.e., "….both the claims and disclosure as originally filed are specifically directed to the use of a (2-imidazolin-2-ylamino)-quinoxaline derivative compound, in particular, brimonidine tartrate, as the alpha-2 adrenergic agonist to be employed in the disclosed method of treatment.") See last full sentence of the paragraph bridging pages 3 and 4.

As discussed above, applicant has amended independent claim 36 so that the composition comprises a single active component that reduces cutaneous facial flushing. The single active component consists of brimonidine tartrate. Therefore the 35 U.S.C. 112, first paragraph, rejection has been rendered moot.

Reconsideration and withdrawal of the 35 U.S.C. 112, first paragraph, rejection is respectfully requested.

35 U.S.C. 103 REJECTION

The examiner maintained the rejections of claims 11, 12, and 36 under 35 U.S.C. 103(a) as being unpatentable over WO 02/36144 (hereinafter "*Arnold*") in view of U.S. Patent Publication No. 2003/0229088 (hereinafter "*Gil*") Wymenga et al., "Management of Hot Flushes in Breast Cancer Patients," *Acta Oncologia 41(3)*:269-275(2002) (hereinafter "*Wymenga*") and EP 1069124 (hereinafter "*Ito*").

According to the examiner, the primary reference, *Arnold*, discloses a medicament useful for treating side effects of ovarectomy or symptoms associated with menopause, wherein such symptoms include vasomotor symptoms, *e.g.*, hot flushes. The medicament includes one or more GnRH analogue compounds. Optionally, other compounds can be included, one of a large number of which are α-adrenergic agonists. (Office action page 5, 1st full paragraph.)

The examiner concedes that *Arnold* does **not** disclose the use of brimonidine tartrate as the α-adrenergic agonist, does **not** disclose topical administration of the medicament locally to the site of the facial flushing, and does not disclose the concomitant use of an additional agent as provided in claim 11. (Office action page 6, 1st full paragraph.)

In an attempt to remedy the deficiencies in *Arnold*, the examiner relies upon *Gil* for allegedly disclosing known α-adrenergic agonists, including clonidine, brimonidine, tizanidine, etc., and salts thereof, in dermatologically acceptable formulations, *e.g.*, a dermal patch, topical drops, creams, gels and ointments. According to the examiner, it would have been obvious to employ brimonidine, or a salt thereof, in the medicament disclosed by *Arnold* because *Gil* discloses that brimonidine is "one of a finite number of α-adrenergic agonists known in the art at the time of the invention to predictably function as an agonist of α-adreno-receptors." (Office action page 6, 3rd paragraph.) The examiner also attempts to rely on *Ito* for the disclosure of treating hot flushes with a composition which may be topically administered.

In order to expedite examination, applicant has limited the main independent claim to the use of a composition containing a single active component that reduces cutaneous facial flushing. The single active component consists of brimonidine tartrate. Accordingly, the composition can only contain one component that reduces the facial flushing. The addition of any other components that reduce facial flushing is excluded by the claim language.

The examiner states the previously filed amendments to the claims would not overcome *Arnold* because "the composition, as a whole, remains open to the inclusion of additional,

unrecited elements as evidenced by the use of the transitional phrase 'comprising.'" (Office action page 5, 2nd full paragraph.)

Applicant understands the examiner's reasoning, and has, therefore, amended independent claim 36 in order to specify that the composition is limited to a single active component that reduces cutaneous facial flushing. The single active component consists of, i.e., is limited to, brimonidine tartrate. See claim 36 reprinted below.

> 36. (Currently Amended) A method of treating facial flushing associated with menopause-associated hot flashes in a human in need thereof, the method comprising topically administering a composition comprising an effective amount of a single active component that~~to~~ reduces cutaneous facial flushing, wherein the single active component consists of ~~brimonidine or~~ brimonidine tartrate~~, or combinations thereof~~, and a dermatologically acceptable carrier, locally to facial skin of the human, wherein the brimonidine tartrate~~single component~~ acts locally to reduce cutaneous facial flushing.

Although the transitional word "comprising" appears after the word "composition," the composition is limited to "a single active component that reduces cutaneous facial flushing, wherein the singe active component consists of brimonidine tartrate…." Therefore, while the composition may contain other ingredients, *e.g.*, non-active dermatologically acceptable excipients, as a result of the inclusive "comprising" language, the other ingredients in the composition cannot be active to reduce cutaneous facial flushing.

Accordingly, independent claim 36 necessarily excludes the use of compositions containing compounds in addition to brimonidine tartrate that reduce cutaneous facial flushing. Accordingly, the primary reference, *Arnold*, does not render the claims obvious because it requires one or more GnRH analogue compound to treat the side effects of ovarectomy or

symptoms associated with menopause. Claim 36 excludes the possibility of one or more GnRH analogue compound being in the claimed composition. Therefore, *Arnold* actually teaches away from the claimed invention.

Applicant believes that the new wording of claim 36 overcomes the 35 U.S.C. 103(a) rejection. If the examiner still has concerns, applicant would welcomes a dialog with the examiner regarding the wording of the claim.

In order for a *prima facie* obviousness rejection to be made, the combined teachings of the references must suggest the claimed invention to one of ordinary skill in the art. None of the references cited by the examiner suggest topical treatment of cutaneous facial flushing with the single active ingredient of brimonidine tartrate. In fact, the primary reference, *Arnold*, teaches away from the claimed invention. Accordingly, applicant respectfully requests withdrawal of the obviousness rejection.

In view of the clear distinction of the presently amended claim over the primary reference, applicant does not consider it necessary to repeat his assertions of the deficiencies of the secondary references. Applicant refers to his previous response if the examiner wishes to review them.

Applicant respectfully submits that the application is now in proper form for allowance, which action is earnestly solicited. If resolution of any remaining issue is required prior to allowance of the application, it is respectfully requested that the examiner contact applicant's attorney at the telephone number provided below.

Respectfully submitted,

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